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## The history of diabetes: From olden days to discovering insulin

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### Abstract

Diabetes is common metabolic disorder which affects larger population of the world. Currently its prevalence is high up and increased day by day. In despite advancement of western science which resist to treat of this silent killer disease. Diabetes characterized by the 'too great emptying of urine' finds its place in antiquity through Egyptian manuscripts dating back to 1500 B.C This article depicted preliminary opinion that diabetes was associated to an alimentary illness, and concludes with the discovery of it being a persistent systemic ailment and described three successive ways. This short review article informs us, how for many centuries peoples are suffered from the devastating illness with very little offered in terms of treatment or relief. After long time the pancreas was identified as the causative organ and, some time later, animal experimentation resulted in the abstraction of the substance insulin.

**Keywords:** Diabetes, ancient period, history of diabetes, insulin era

### Introduction

Diabetes is a group of chronic diseases characterized by hyperglycemia. <sup>[1]</sup> The long-term effects of diabetes include damage, dysfunction, and failure of various organs. <sup>[2]</sup> Indian physicians called it madhumeha ('honey urine') because it attracted ants. The ancient Indian physician, Sushruta, and the surgeon Charaka (400–500 A.D.) were able to identify the two types, later to be named Type I and Type II diabetes. <sup>[3]</sup> Unani Physicians termed the disease "Al-dulab" (wheel of water) and "Zalqul Kulliya" (diarrhea of the kidneys), these terms also used by Galen. <sup>[4]</sup>

### Historical Background

**Ancient Period:** Clinical aspect alike to diabetes mellitus was explained 3000 years ago by the ancient Egyptians <sup>[5]</sup>. In Egypt, the first written documents described diabetes in the *Eberes papyrus* by George Eberes dated back to 1550 BC, as polyuria which is similar to diabetes <sup>[6]</sup>. Although Greek physician Hippocrates (460 BC) the father of medicine did not specifically mention diabetes in his writings, there are elucidate in the Hippocratic writings that are reliable with the sign and symptoms of diabetes. There are sources to excessive urinary flow with wasting of the body <sup>[7]</sup>. The first entire clinical explanation of diabetes emerges to have been made by Aulus Cornelius Celsus (30BC–50 AD). Often called "Cicero medicorum" for his elegant Latin, Celsus included the explanation of diabetes in his monumental eight-volume work entitled *De medicina* <sup>[8]</sup>. The term "diabetes" (Greek-Siphon or 'diabainein') was first time coined by Araetus of Cappodocia (81-133AD) and dramatically stated "no essential part of the drink is absorbed by the body while great masses of the flesh are limbs (liquefied) into urine" <sup>[5, 9]</sup>. Galen, a Roman physician, observed that diabetes was a rare ailment as he had seen only two cases during their clinical observation. He mentioned the development of diabetes is due to weakness of the kidney and gave it a name "diarrhea of the urine" ("diarrhea urinosa") and the thirsty disease (dipsakos) <sup>[7, 8, 10]</sup>. Chinese (Chang Chung-Ching in 229 AD) and Japanese (Li Hsuan) literature explained a disease with sweet urine which attracted dogs and insects. Such patients were more prone to develop boils and tuberculosis <sup>[11, 12]</sup>. Ancient Indian physicians Susruta, Charaka and Vaghbata described during 5<sup>th</sup> and 6<sup>th</sup> A.D, sweet taste of urine in polyuric younger patients and named it as "Madhumeha (honey urine)" and were able to identify two types of diabetes, later to be named type-I and type-II diabetes <sup>[8, 9]</sup>. *Ibn Sina* (980-1037), who termed the disease "Al-dulab" (wheel of water) and "Zalqul Kulliya" (diarrhea of the kidneys), these terms also used by Galen <sup>[4]</sup>.

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## Diabetes- A Disease of the Kidney

The first paradigm shift in the conceptual evolution of diabetes comes from the studies of Paracelsus (1493-1541) who describes it as a constitutional disease that “irritates the kidneys” and provokes excessive urination. Having evaporated the urine from a diabetic patient, Paracelsus reported an excessive residue, which he called “salts,” and described diabetes as an affection of the blood “being involved with salt particles, do run forth through the most open passages of the Reins (kidneys) [13, 14, 15, 16].

**Diagnostic period:** In 1675 AD Thomas Willis – added the word ‘mellitus’ (from the Latin of honey) to refer to the sweet taste of urine. In 1776 AD Matthew Dobson – confirmed that sugar was present in both the urine and blood of diabetic individuals. Early 18<sup>th</sup> Claude Bernard – hypothesised that glycogen was stored by the liver and secreted as a sugary substance into the blood. Overproduction of glucose was considered to be the cause of diabetes [6, 8].

## Diabetes- A Disease of the Pancreas

In 1788 AD Thomas Cawley discovered correlation between shrivelled pancreas and diabetic individuals. 1889 AD Joseph von Mering and Oscar Minkowski discovered the removal of a pancreas from a dog led to diabetes. 1893 AD Gustave Edouard Laguesse suggested that pancreatic islet cells were involved in diabetes, and named them the Islets of Langerhans. In 1894 A.D. Moses Barron linked damaged Islets of Langerhans to the cause of diabetes, and surmised that the substance from these cells was the treatment for diabetes [6, 8]. The specific role of the pancreas was further refined after Paul Langerhans (1849-1888) described in 1869 the unique morphologic features of the pancreatic islands that were subsequently named after him. In 1909, Eugene L. Opie (1873-1971) reported hyaline degeneration of the islands in diabetic patients, a finding subsequently confirmed in a series of experimental studies that led Edward Sharpey-Schafer to suggest in 1916 that the islands of Langerhans produced a glucose regulating hormone that he termed insulin. The race for isolating the hypothesized hormone was now on. Frederick Banting (1891- 1941) and Charles Best (1892-1978) finally did so in 1922. They wanted to call it isletin, but J.J.R Macleod (1876-1935), in whose laboratory their work was done, insisted on using insulin. The endocrine nature of diabetes was now clearly established. The stage of diabetes as a disease of the kidneys was over [6].

**Insulin Era:** Insulin term (derived from latin word insula or island) is given by Jean de Mayer, a Belgian physician in 1909 to the glucose-lowering hormone. de Mayer postulated that this hormone was produced by the islet tissues. In December 1921, Banting and Macleod succeeded in isolating insulin; a milestone event. On 11<sup>th</sup> January 1922, 14 year old diabetic boy named Leonard Thomson was treated with insulin first time. They were awarded Noble prize for that in 1923 [10]. In 1923, Eli Lilly begins commercial production of insulin (Isletin Insulin). In 1925, Home testing for sugar in urine through Benedict’s solution was introduced. In 1926, John Jacob Abel purified insulin, isolated its crystalline structure and hence chemically identified. In 1927, an oral medication “horment” or “gluko horment” was developed as a replacement for insulin, but dropped out due to its side effects. In 1928, Wintersteiner and his colleagues described insulin as a protein composed of amino acids. In 1930s, Insulin was further refined to Protamine zinc insulin, a long-acting insulin. Insulin therapy soon became backbone of management that enabled individuals affected by this disease to live an almost-normal life. It soon became apparent that insulin did not cure diabetes. As people began to live longer, they experienced complications that had not previously been seen. In 1936 Himsworth proposed two types of diabetes as insulin sensitive and insulin insensitive, former being due to insulin deficiency. This observation laid the foundation for the concept of impaired insulin action, which is now known to be a crucial factor in pathogenesis of type 2 diabetes. In 1923, Collip found that onion has a hypoglycemic effect in fasting and depancreatized animals. The first oral hypoglycemic agent sulfonylurea was discovered in 1942 by M.J. Janbon. Franke and Fuchs in Berlin applied it clinically [8, 16]. In 1980, the first human insulin was manufactured by Graham Bell. In 1982, the first biosynthetic insulin (humulin) was developed. Syringes appeared in 1961 but,

being made of glass, brought with them the attendant hazards of infections until they were replaced with disposable plastic ones. It was only 15 years later that the introduction of the first needle-free insulin delivery system by Derata in 1979 provided relatively pain free, metered doses [9].

**Concept of *Ziabetus*:** The term “Diabetes” is derived from Greek word “*diabainein*” which means “passing through” or “to run through” or Siphon.” It is characterized by excessive thirst, excessive urination, presence of sugar in urine, increased appetite and gradual loss of body weight etc [6, 9]. *Ziabetus* is revealed in nearly all of the Unani text like *Al-Hawi*, *Kamilul Sana’ah*, *Al-Qanoon*, *Zakheera Khwarzam shahi* etc. Unani physicians mentioned that *Ziabetus* is a disease of kidneys. Arabic physicians had depicted *Ziabetus* by several other terms viz; *Moattasha*, *Atsha*, *Intesae Anmas*, *Zalaqul kulliya*, *Dolab*, *Dawwarah*, *Barkar*, *Barkarya*, *Qaramees* etc [17-27]. According to Unani medicine, *Ziabetus Shakri* is an ailment in which the consumed water is passed out through the kidney instantly after drinking by the patient. It resembles to *Zalqul Meda wal Ama*, in which the food passes swiftly through the stomach and intestine lacking proper digestion. In this ailment patient has excessive thirst and takes plenty of water and passes all the water he consumed without any metabolic change [17-27]. In this disease *Mizaj* of kidneys become *Haar* so they absorb water from blood and send to the urinary bladder immediately due to weakness in *Quwate Masika* (retentive power). It also been described that the kidneys attract the watery substance of blood, but the urinary bladder does not attract any thing. So kidneys attract the water from the circulation, liver, stomach and intestines because of that patient have the immoderate thirst (polydipsia) [17-27].

### Conclusion

This review article, gives a historical explanation of events for diabetes, dating from ancient times and it’s first documentation by Ebers Papyrus in 1500 BC which explains initial thoughts that diabetes was connected to an alimentary disease. This article tells how far many centuries peoples suffered from the devastating complaint with very little existing treatment or relief. We authors concluded that disease and their treatment methodology vary from time to time in successive manner with development of scientific research.

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